Remarks

Claims 17-19, 21 and 30 are now in the case. Claims 22-28 are withdrawn as being drawn to a non-elected invention. Claims 1-16, 20 and 29 are cancelled. Claims 17-18 are amended. Claim 30 is added. Support for the amendments can be found in the claims as originally filed and through out the application, see in particular, page 8 and Example 2. No new matter has been added.

Specification

The priority claim has been amended to indicate the status of the parent application (US Patent Application No. 09/561,779) as abandoned.

The specification has also been amended to remove the use of brackets on page 11 and hyperlinks or other forms of browser-executable code on pages 3-4.

Election/Restrictions

Office states Inventions of Groups 1 and 2 are unrelated, each to the other, because each comprises a distinct product having a unique primary structure and because the protease of Group 2 is disclosed to have a different catalytic function than the polypeptide of Group 1. Group 1 comprises claims 13-21 and 29. Claim 13 recited a substantially purified polypeptide having disintegrin activity and comprising an amino acid sequence having at least 80% identity across the length of amino acids 399 through 502 of SEQ ID NO:2.

Group 2 comprises claims 22-28. Claim 22 is directed to an isolated polynucleotide encoding the polypeptide of claim 13. Claims 23-25, 27 all depend from claim 22, claims 24 and 28 depend directly from a claim depending from Claim 22.

The assertion by the Office that the protease of Group 2 has different catalytic function than the polypeptide of Group 1 has no basis because the polypeptides of Group 2 encode the polypeptides of Group 1. Therefore Applicant requests that the claims of Groups 1 and 2 be recombined.

Applicant affirms the election, with traverse, of Group 1, claims 13-21 and 29.

Rejection under 35 U.S.C. § 101 and § 112, first paragraph:

Claims 13-21 and 29 are rejected under 35 U.S.C. § 101 and § 112, first paragraph because the claimed invention allegedly lacks patentable utility.

Applicant respectfully traverses these grounds for rejection. However, merely to advance prosecution of the pending claims, claims 13-16, 18, 20 and 29 have been cancelled.

Claim 18 has been amended to depend from new claim 30. Applicant reserves the right to pursue the cancelled matter in continuation applications.

The Office asserts no specific *in vitro* or *in vivo* utility; no specific or generic biological activity for the disintegrin domain is set forth.

Applicant's claimed polypeptide is a member of a protein family identified as ADAMs, a distinguishing characteristic of this family is the presence of an integrin-binding disintegrin domain. Integrins are a family of cell adhesion receptors that bind various ligands including cell surface molecules. Integrins are involved in cell-cell and cell-matrix interactions and inflammatory responses. Integrins are found on the surface of various cells and along with their binding partners, play a role in biological processes including embryonic development, platelet aggregation, immune reactions, tissue repair and remodeling, bone resorption, tumor invasion and metastasis and are targets for therapeutic intervention in human disease.

The binding of disintegrin domains to integrins makes disintegrin domain proteins very useful as tools and/or therapeutics. For example, binding of disintegrin domains to integrins has been shown to be responsible for such cell-cell interactions as egg-sperm fusion, muscle cell fusion, and neurogenesis and axonal extension (page 9, lines 16-19). Agents comprising a disintegrin domain can be used to disrupt normal cell-cell and cell-matrix interactions by inhibiting the binding of cell surface integrins to their disintegrin domain ligands. For example, soluble disintegrin domains, such as the disintegrin domain containing Fc fusion protein identified in SEQ ID NO:3 and Example 2, can be used to inhibit the interaction of integrins and their ligands. Target-specific inhibitory or agonistic agents are well known and routinely sought and relied upon by those in the art.

Mammalian fertilization involves a cascade of cell-cell interactions. Disintegrin domains of fertilins are found on the sperm surface are involved in binding and fusion with integrins on the egg plasma membrane. Fertilin-α/ADAM1 and fertilin-β/ADAM2 are required for sperm-egg function. "Fertilin is the prototype of a growing and widely distributed family (ADAMs) of membrane proteins that possess an integrin ligand domain with the disintegrin motif.... Hence, a direct interaction between ADAMs and integrins might represent a novel type of cell-cell interaction used not only for sperm-egg binding, but other important cell-cell recognition ... and signaling events." (see page 1101, last full paragraph, left column, Almeida et al., *Cell* 81:1095-1104, 1996, emphasis added, a copy is provided herein).

ADAM polypeptides most similar to SVPH1-26 include ADAMs1-6, and 16, for example, are known to those in the art as implicated in fertilization and/or spermatogenesis (specification, paragraph bridging pages 8-9), and ADAM12 (meltrin alpha) is involved in a cell-cell fusion process analogous to fertilization: fusion of myoblasts into muscle cells (specification, page 9, lines 16-17). In addition, the specification teaches in Example 1 on page 58 that SVPH1-26 mRNA was detected only in testis tissue, and that this "finding that SVPH1-26 is specifically expressed in testis by Northern analysis also implicates this family member in fertilization and/or spermatogenesis" (page 9, lines 3-4).

Utility under 35 U.S.C. §101 is a minimal threshold issue that can be satisfied by a showing of any use that is "credible," "specific" and "substantial" (MPEP §2107). A small degree of utility is sufficient. Thus, as a matter of Patent Office practice, a specification that provides disclosure of a utility that corresponds in scope to the subject matter sought to be patented and that is substantial, credible, and specific must be taken as sufficient to satisfy the utility requirement of 35 U.S.C. §101 for the entire claimed subject matter unless there is reason for one skilled in the art to question the objective truth of the statement of utility.

SVPH1-26 is an ADAM protein and like all other ADAMs has a disintegrin domain that binds integrins. The usefulness of such integrin-binding proteins is acknowledged in the art. Like the majority of known ADAMs, SVPH1-26 is associated with and is predominantly expressed on testis tissue. Testis-expressed ADAM proteins are known to bind to egg-expressed integrin proteins, thereby participating in the fusion of sperm and egg cells and contributing to fertilization and reproduction. The integrin binding activity of disintegrin domains of ADAM proteins is useful and desirable.

Therefore, the claimed polypeptides are useful, in part, due to the specificity of the disintegrin domain as an integrin binding partner. The uses of such integrin binding proteins are credible. "The observation that fertilin β possesses a disintegrin domain...led us to predict that an integrin on the egg plasma membrane could serve as a sperm receptor." Almeida et al., first line, paragraph bridging pages 1095-1095). One of skill has an appreciation of the usefulness of disintegrin domain-containing ADAM proteins, such as SVPH1-26. "We propose that binding between fertilins and integrins may provide a general mechanism for adhesion among mammalian gametes." Alemida et al., page 1101, second paragraph, left-hand column). This usefulness of proteins that bind integrins is also substantial in that there are real world applications associated with embryonic development, platelet aggregation, immune reactions, tissue repair and remodeling, bone resorption, tumor invasion and metastasis, for example.

As discussed above, integrins are involved in cell-cell interactions and as such play an important role in biological processes and are important targets for therapeutic intervention in human disease. Mammalian fertilization involves a cascade of cell-cell interactions. The disintegrin domains of similarly expressed ADAMs are involved in binding and fusion with integrins on the egg plasma membrane. SVPH1-26 is predominantly expressed in testis tissue. Applicant, like those of skill in the art, appreciate the usefulness of an integrin-binding protein, particularly one that is predominantly expressed in a critical tissue and anticipated that use may be made of the disintegrin domain and its integrin binding properties. Likewise, soluble disintegrin domain proteins are useful for binding integrins expressed on other tissues.

The usefulness of such integrin binding proteins would be readily apparent to one of skill in the art and application of such proteins is credible, specific and substantial.

Therefore, for at least the reasons presented above, Applicant has asserted in the specification a specific, substantial, and credible use for compositions of matter of the invention, and withdrawal of the rejection of claims 13-21 and 29 under 35 U.S.C. §101 and §112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph (written description):

Claims 13-16, 18, 20 and 29 are rejected under § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Office asserts that the specification fails to exemplify or describe the preparation of the divergent amino acid sequences of variant disintegrin domains of claims 13-16, 18, 20 and 29.

Applicant respectfully traverses these grounds for rejection. However, as noted above claims 13-16, 20 and 29 have been cancelled. Claim 18 has been amended to depend from new claim 30.

Applicant respectfully submits that for at least the reasons stated above, the rejection of claims 13-16, 18, 20 and 29 under 35 U.S.C. §112, first paragraph (written description), is moot and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph (enablement):

Claims 13-16, 18, 20 and 29 are rejected under § 112, first paragraph, because the specification, while being enabling for the preparation of a disintegrin domain having

disintegrin activity comprising either an amino acid sequence identical to the 104-amino acid sequence between amino acid residues 399-502, inclusive of SEQ ID NO:2 or the amino acid sequence set forth in SEQ ID NO:3, does not reasonably provide enablement for divergent sequences.

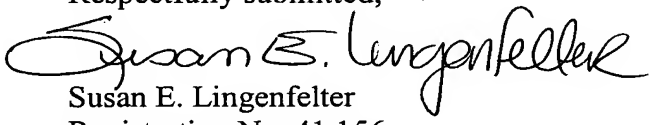
Applicant respectfully traverses these grounds for rejection. However, as described above, claims 13-16, 20 and 29 have been cancelled. Claim 18 has been amended to depend from new claim 30.

Applicant respectfully submits that for at least the reasons stated above, the rejection of claims 13-16, 18, 20 and 29 under 35 U.S.C. §112, first paragraph (enablement), is moot and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicant submits that the presented claims are in condition for allowance. A favorable action is earnestly requested. Applicant's attorney invites the Examiner to call her at the number below if any issue remains outstanding.

Respectfully submitted,



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